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```
ACCCACGCGC AGCGGCCGGA G ATG CAG CGG GGC GCC GCG CTG TGC CTG CGA   51
                        Met Gln Arg Gly Ala Ala Leu Cys Leu Arg
                         1               5                  10

CTG ACC CCC CCG ACC TTG AAC ATC ACG GAG GAG TCA CAC GTC ATC GAC   99
Leu Trp Leu Cys Leu Gly Leu Leu Asp Gly Leu Val Ser Asp Tyr Ser
                15                  20                  25

ATG ACC CCC CCG ACC TTG AAC ATC ACG GAG GAG TCA CAC GTC ATC GAC  147
Met Thr Pro Pro Thr Leu Asn Ile Thr Glu Glu Ser His Val Ile Asp
            30                  35                  40

ACC GGT GAC AGC CTG TCC ATC TCC TGC AGG GGA CAG CAC CCC CTC GAG  195
Thr Gly Asp Ser Leu Ser Ile Ser Cys Arg Gly Gln His Pro Leu Glu
        45                  50                  55

TGG GCT TGG CCA GGA GCT CAG GAG GCG CCA GCC ACC GGA GAC AAG GAC  243
Trp Ala Trp Pro Gly Ala Gln Glu Ala Pro Ala Thr Gly Asp Lys Asp
    60                  65                  70

AGC GAG GAC ACG GGG GTG GTG CGA GAC TGC GAG GGC ACA GAC GCC AGG  291
Ser Glu Asp Thr Gly Val Val Arg Asp Cys Glu Gly Thr Asp Ala Arg
75                  80                  85                  90

CCC TAC TGC AAG GTG TTG CTG CTG CAC GAG GTA CAT GCC AAC GAC ACA  339
Pro Tyr Cys Lys Val Leu Leu Leu His Glu Val His Ala Asn Asp Thr
                95                 100                 105

GGC AGC TAC GTC TGC TAC TAC AAG TAC ATC AAG GCA CGC ATC GAG GGC  387
Gly Ser Tyr Val Cys Tyr Tyr Lys Tyr Ile Lys Ala Arg Ile Glu Gly
            110                 115                 120

ACC ACG GCC GCC AGC TCC TAC GTG TTC GTG AGA GAC TTT GAG CAG CCA  435
Thr Thr Ala Ala Ser Ser Tyr Val Phe Val Arg Asp Phe Glu Gln Pro
        125                 130                 135

TTC ATC AAC AAG CCT GAC ACG CTC TTG GTC AAC AGG AAG GAC GCC ATG  483
Phe Ile Asn Lys Pro Asp Thr Leu Leu Val Asn Arg Lys Asp Ala Met
    140                 145                 150

TGG GTG CCC TGT CTG GTG TCC ATC CCC GGC CTC AAT GTC ACG CTG CGC  531
Trp Val Pro Cys Leu Val Ser Ile Pro Gly Leu Asn Val Thr Leu Arg
155                 160                 165                 170

TCG CAA AGC TCG GTG CTG TGG CCA GAC GGG CAG GAG GTG GTG TGG GAT  579
Ser Gln Ser Ser Val Leu Trp Pro Asp Gly Gln Glu Val Val Trp Asp
                175                 180                 185

GAC CGG CGG GGC ATG CTC GTG TCC ACG CCA CTG CTG CAC GAT GCC CTG  627
Asp Arg Arg Gly Met Leu Val Ser Thr Pro Leu Leu His Asp Ala Leu
            190                 195                 200

TAC CTG CAG TGC GAG ACC ACC TGG GGA GAC CAG GAC TTC CTT TCC AAC  675
Tyr Leu Gln Cys Glu Thr Thr Trp Gly Asp Gln Asp Phe Leu Ser Asn
        205                 210                 215
```

FIG. 1A

```
CCC TTC CTG GTG CAC ATC ACA GGC AAC GAG CTC TAT GAC ATC CAG CTG   723
Pro Phe Leu Val His Ile Thr Gly Asn Glu Leu Tyr Asp Ile Gln Leu
    220                 225                 230

TTG CCC AGG AAG TCG CTG GAG CTG CTG GTA GGG GAG AAG CTG GTC CTC   771
Leu Pro Arg Lys Ser Leu Glu Leu Leu Val Gly Glu Lys Leu Val Leu
235                 240                 245                 250

AAC TGC ACC GTG TGG GCT GAG TTT AAC TCA GGT GTC ACC TTT GAC TGG   819
Asn Cys Thr Val Trp Ala Glu Phe Asn Ser Gly Val Thr Phe Asp Trp
                255                 260                 265

GAC TAC CCA GGG AAG CAG GCA GAG CGG GGT AAG TGG GTG CCC GAG CGA   867
Asp Tyr Pro Gly Lys Gln Ala Glu Arg Gly Lys Trp Val Pro Glu Arg
            270                 275                 280

CGC TCC CAA CAG ACC CAC ACA GAA CTC TCC AGC ATC CTG ACC ATC CAC   915
Arg Ser Gln Gln Thr His Thr Glu Leu Ser Ser Ile Leu Thr Ile His
        285                 290                 295

AAC GTC AGC CAG CAC GAC CTG GGC TCG TAT GTG TGC AAG GCC AAC AAC   963
Asn Val Ser Gln His Asp Leu Gly Ser Tyr Val Cys Lys Ala Asn Asn
    300                 305                 310

GGC ATC CAG CGA TTT CGG GAG AGC ACC GAG GTC ATT GTG CAT GAA AAT  1011
Gly Ile Gln Arg Phe Arg Glu Ser Thr Glu Val Ile Val His Glu Asn
315                 320                 325                 330

CCC TTC ATC AGC GTC GAG TGG CTC AAA GGA CCC ATC CTG GAG GCC ACG  1059
Pro Phe Ile Ser Val Glu Trp Leu Lys Gly Pro Ile Leu Glu Ala Thr
                335                 340                 345

GCA GGA GAC GAG CTG GTG AAG CTG CCC GTG AAG CTG GCA GCG TAC CCC  1107
Ala Gly Asp Glu Leu Val Lys Leu Pro Val Lys Leu Ala Ala Tyr Pro
            350                 355                 360

CCG CCC GAG TTC CAG TGG TAC AAG GAT GGA AAG GCA CTG TCC GGG CGC  1155
Pro Pro Glu Phe Gln Trp Tyr Lys Asp Gly Lys Ala Leu Ser Gly Arg
        365                 370                 375

CAC AGT CCA CAT GCC CTG GTG CTC AAG GAG GTG ACA GAG GCC AGC ACA  1203
His Ser Pro His Ala Leu Val Leu Lys Glu Val Thr Glu Ala Ser Thr
    380                 385                 390

GGC ACC TAC ACC CTC GCC CTG TGG AAC TCC GCT GCT GGC CTG AGG CGC  1251
Gly Thr Tyr Thr Leu Ala Leu Trp Asn Ser Ala Ala Gly Leu Arg Arg
395                 400                 405                 410

AAC ATC AGC CTG GAG CTG GTG GTG AAT GTG CCC CCC CAG ATA CAT GAG  1299
Asn Ile Ser Leu Glu Leu Val Val Asn Val Pro Pro Gln Ile His Glu
                415                 420                 425

AAG GAG GCC TCC TCC CCC AGC ATC TAC TCG CGT CAC AGC CGC CAG GCC  1347
Lys Glu Ala Ser Ser Pro Ser Ile Tyr Ser Arg His Ser Arg Gln Ala
            430                 435                 440
```

FIG. 1B

```
CTC ACC TGC ACG GCC TAC GGG GTG CCC CTG CCT CTC AGC ATC CAG TGG  1395
Leu Thr Cys Thr Ala Tyr Gly Val Pro Leu Pro Leu Ser Ile Gln Trp
        445                 450                 455

CAC TGG CGG CCC TGG ACA CCC TGC AAG ATG TTT GCC CAG CGT AGT CTC  1443
His Trp Arg Pro Trp Thr Pro Cys Lys Met Phe Ala Gln Arg Ser Leu
    460                 465                 470

CGG CGG CGG CAG CAG CAA GAC CTC ATG CCA CAG TGC CGT GAC TGG AGG  1491
Arg Arg Arg Gln Gln Gln Asp Leu Met Pro Gln Cys Arg Asp Trp Arg
475                 480                 485                 490

GCG GTG ACC ACG CAG GAT GCC GTG AAC CCC ATC GAG AGC CTG GAC ACC  1539
Ala Val Thr Thr Gln Asp Ala Val Asn Pro Ile Glu Ser Leu Asp Thr
                495                 500                 505

TGG ACC GAG TTT GTG GAG GGA AAG AAT AAG ACT GTG AGC AAG CTG GTG  1587
Trp Thr Glu Phe Val Glu Gly Lys Asn Lys Thr Val Ser Lys Leu Val
            510                 515                 520

ATC CAG AAT GCC AAC GTG TCT GCC ATG TAC AAG TGT GTG GTC TCC AAC  1635
Ile Gln Asn Ala Asn Val Ser Ala Met Tyr Lys Cys Val Val Ser Asn
        525                 530                 535

AAG GTG GGC CAG GAT GAG CGG CTC ATC TAC TTC TAT GTG ACC ACC ATC  1683
Lys Lys Gly Gln Asp Glu Arg Leu Ile Tyr Phe Tyr Val Thr Thr Ile
    540                 545                 550

CCC GAC GGC TTC ACC ATC GAA TCC AAG CCA TCC GAG GAG CTA CTA GAG  1731
Pro Asp Gly Phe Thr Ile Glu Ser Lys Pro Ser Glu Glu Leu Leu Glu
555                 560                 565                 570

GGC CAG CCG GTG CTC CTG AGC TGC CAA GCC GAC AGC TAC AAG TAC GAG  1779
Gly Gln Pro Val Leu Leu Ser Cys Gln Ala Asp Ser Tyr Lys Tyr Glu
                575                 580                 585

CAT CTG CGC TGG TAC CGC CTC AAC CTG TCC ACG CTG CAC GAT GCG CAC  1827
His Leu Arg Trp Tyr Arg Leu Asn Leu Ser Thr Leu His Asp Ala His
            590                 595                 600

GGG AAC CCG CTT CTG CTC GAC TGC AAG AAC GTG CAT CTG TTC GCC ACC  1875
Gly Asn Pro Leu Leu Leu Asp Cys Lys Asn Val His Leu Phe Ala Thr
        605                 610                 615

CCT CTG GCC GCC AGC CTG GAG GAG GTG GCA CCT GGG GCG CGC CAC GCC  1923
Pro Leu Ala Ala Ser Leu Glu Glu Val Ala Pro Gly Ala Arg His Ala
    620                 625                 630

ACG CTC AGC CTG AGT ATC CCC CGC GTC GCG CCC GAG CAC GAG GGC CAC  1971
Thr Leu Ser Leu Ser Ile Pro Arg Val Ala Pro Glu His Glu Gly His
635                 640                 645                 650

TAT GTG TGC GAA GTG CAA GAC CGG CGC AGC CAT GAC AAG CAC TGC CAC  2019
Tyr Val Cys Glu Val Gln Asp Arg Arg Ser His Asp Lys His Cys His
                655                 660                 665
```

FIG. 1C

```
AAG AAG TAC CTG TCG GTG CAG GCC CTG GAA GCC CCT CGG CTC ACG CAG  2067
Lys Lys Tyr Leu Ser Val Gln Ala Leu Glu Ala Pro Arg Leu Thr Gln
            670                 675                 680

AAC TTG ACC GAC CTC CTG GTG AAC GTG AGC GAC TCG CTG GAG ATG CAG  2115
Asn Leu Thr Asp Leu Leu Val Asn Val Ser Asp Ser Leu Glu Met Gln
        685                 690                 695

TGC TTG GTG GCC GGA GCG CAC GCG CCC AGC ATC GTG TGG TAC AAA GAC  2163
Cys Leu Val Ala Gly Ala His Ala Pro Ser Ile Val Trp Tyr Lys Asp
    700                 705                 710

GAG AGG CTG CTG GAG GAA AAG TCT GGA GTC GAC TTG GCG GAC TCC AAC  2211
Glu Arg Leu Leu Glu Glu Lys Ser Gly Val Asp Leu Ala Asp Ser Asn
715                 720                 725                 730

CAG AAG CTG AGC ATC CAG CGC GTG GCG GAG GAG GAT GCG GGA CCG TAT  2259
Gln Lys Leu Ser Ile Gln Arg Val Arg Glu Glu Asp Ala Gly Pro Tyr
                735                 740                 745

CTG TGC AGC GTG TGC AGA CCC AAG GGC TGC GTC AAC TCC TCC GCC AGC  2307
Leu Cys Ser Val Cys Arg Pro Lys Gly Cys Val Asn Ser Ser Ala Ser
            750                 755                 760

GTG GCC GTG GAA GGC TCC GAG GAT AAG GGC AGC ATG GAG ATC GTG ATC  2355
Val Ala Val Glu Gly Ser Glu Asp Lys Gly Ser Met Glu Ile Val Ile
        765                 770                 775

CTT GTC GGT ACC GGC GTC ATC GCT GTC TTC TTC TGG GTC CTC CTC CTC  2403
Leu Val Gly Thr Gly Val Ile Ala Val Phe Phe Trp Val Leu Leu Leu
    780                 785                 790

CTC ATC TTC TGT AAC ATG AGG AGG CCG GCC CAC GCA GAC ATC AAG ACG  2451
Leu Ile Phe Cys Asn Met Arg Arg Pro Ala His Ala Asp Ile Lys Thr
795                 800                 805                 810

GGC TAC CTG TCC ATC ATC ATG GAC CCC GGG GAG GTG CCT CTG GAG GAG  2499
Gly Tyr Leu Ser Ile Ile Met Asp Pro Gly Glu Val Pro Leu Glu Glu
                815                 820                 825

CAA TGC GAA TAC CTG TCC TAC GAT GCC AGC CAG TGG GAA TTC CCC CGA  2547
Gln Cys Glu Tyr Leu Ser Tyr Asp Ala Ser Gln Trp Glu Phe Pro Arg
            830                 835                 840

GAG CGG CTG CAC CTG GGG AGA GTG CTC GGC TAC GGC GCC TTC GGG AAG  2595
Glu Arg Leu His Leu Gly Arg Val Leu Gly Tyr Gly Ala Phe Gly Lys
        845                 850                 855

GTG GTG GAA GCC TCC GCT TTC GGC ATC CAC AAG GGC AGC AGC TGT GAC  2643
Val Val Glu Ala Ser Ala Phe Gly Ile His Lys Gly Ser Ser Cys Asp
    860                 865                 870

ACC GTG GCC GTG AAA ATG CTG AAA GAG GGC GCC ACG GCC AGC GAG CAG  2691
Thr Val Ala Val Lys Met Leu Lys Glu Gly Ala Thr Ala Ser Glu Gln
875                 880                 890
```

FIG. 1D

```
CGC GCG CTG ATG TCG GAG CTC AAG ATC CTC ATT CAC ATC GGC AAC CAC 2739
Arg Ala Leu Met Ser Glu Leu Lys Ile Leu Ile His Ile Gly Asn His
                895                 900                 905

CTC AAC GTG GTC AAC CTC CTC GGG GCG TGC ACC AAG CCG CAG GGC CCC 2787
Leu Asn Val Val Asn Leu Leu Gly Ala Cys Thr Lys Pro Gln Gly Pro
            910                 915                 920

CTC ATG GTG ATC GTG GAG TTC TGC AAG TAC GGC AAC CTC TCC AAC TTC 2835
Leu Met Val Ile Val Glu Phe Cys Lys Tyr Gly Asn Leu Ser Asn Phe
        925                 930                 935

CTG CGC GCC AAG CGG GAC GCC TTC AGC CCC TGC GCG GAG AAG TCT CCC 2883
Leu Arg Ala Lys Arg Asp Ala Phe Ser Pro Cys Ala Glu Lys Ser Pro
    940                 945                 950

GAG CAG CGC GGA CGC TTC CGC GCC ATG GTG GAG CTC GCC AGG CTG GAT 2931
Glu Gln Arg Gly Arg Phe Arg Ala Met Val Glu Leu Ala Arg Leu Asp
955                 960                 965                 970

CGG AGG CGG CCG GGG AGC AGC GAC AGG GTC CTC TTC GCG CGG TTC TCG 2979
Arg Arg Arg Pro Gly Ser Ser Asp Arg Val Leu Phe Ala Arg Phe Ser
                975                 980                 985

AAG ACC GAG GGC GGA GCG AGG CGG GCT TCT CCA GAC CAA GAA GCT GAG 3027
Lys Thr Glu Gly Gly Ala Arg Arg Ala Ser Pro Asp Gln Glu Ala Glu
            990                 995                1000

GAC CTG TGG CTG AGC CCG CTG ACC ATG GAA GAT CTT GTC TGC TAC AGC 3075
Asp Leu Trp Leu Ser Pro Leu Thr Met Glu Asp Leu Val Cys Tyr Ser
        1005                1010                1015

TTC CAG GTG GCC AGA GGG ATG GAG TTC CTG GCT TCC CGA AAG TGC ATC 3123
Phe Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Arg Lys Cys Ile
    1020                1025                1030

CAC AGA GAC CTG GCT GCT CGG AAC ATT CTG CTG TCG GAA AGC GAC GTG 3171
His Arg Asp Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Ser Asp Val
1035                1040                1045                1050

GTG AAG ATC TGT GAC TTT GGC CTT GCC CGG GAC ATC TAC AAA GAC CCC 3219
Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro
                1055                1060                1065

GAC TAC GTC CGC AAG GGC AGT GCC CGG CTG CCC CTG AAG TGG ATG GCC 3267
Asp Tyr Val Arg Lys Gly Ser Ala Arg Leu Pro Leu Lys Trp Met Ala
            1070                1075                1080

CCT GAA AGC ATC TTC GAC AAG GTG TAC ACC ACG CAG AGT GAC GTG TGG 3315
Pro Glu Ser Ile Phe Asp Lys Val Tyr Thr Thr Gln Ser Asp Val Trp
        1085                1090                1095

TCC TTT GGG GTG CTT CTC TGG GAG ATC TTC TCT CTG GGG GCC TCC CCG 3363
Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro
    1100                1105                1110
```

FIG. 1E

```
TAC CCT GGG GTG CAG ATC AAT GAG GAG TTC TGC CAG CGC GTG AGA GAC   3411
Tyr Pro Gly Val Gln Ile Asn Glu Glu Phe Cys Gln Arg Val Arg Asp
1115                1120                1125                1130

GGC ACA AGG ATG AGG GCC CCG GAG CTG GCC ACT CCC GCC ATA CGC CAC   3459
Gly Thr Arg Met Arg Ala Pro Glu Leu Ala Thr Pro Ala Ile Arg His
                1135                1140                1145

ATC ATG CTG AAC TGC TGG TCC GGA GAC CCC AAG GCG AGA CCT GCA TTC   3507
Ile Met Leu Asn Cys Trp Ser Gly Asp Pro Lys Ala Arg Pro Ala Phe
            1150                1155                1160

TGC GAC CTG GTG GAG ATC CTG GGG GAC CTG CTC CAG GGC AGG GGC CTG   3555
Ser Asp Leu Val Glu Ile Leu Gly Asp Leu Leu Gln Gly Arg Gly Leu
        1165                1170                1175

CAA GAG GAA GAG GAG GTC TGC ATG GCC CCG CGC AGC TCT CAG AGA TCA   3603
Gln Glu Glu Glu Glu Val Cys Met Ala Pro Arg Ser Ser Gln Ser Ser
    1180                1185                1190

GAA GAG GGC AGC TTC TCG CAG GTG TCC ACC ATG GCC CTA CAC ATC GCC   3651
Glu Glu Gly Ser Phe Ser Gln Val Ser Thr Met Ala Leu His Ile Ala
1195                1200                1205                1210

CAG GCT GAC GCT GAG GAC AGC CCG CCA AGC CTG CAG CGC CAC AGC CTG   3699
Gln Ala Asp Ala Glu Asp Ser Pro Pro Ser Leu Gln Arg His Ser Leu
                1215                1220                1225

GCC GCC AGG TAT TAC AAC TGG GTG TCC TTT CCC GGG TGC CTG GCC AGA   3747
Ala Ala Arg Tyr Tyr Asn Trp Val Ser Phe Pro Gly Cys Leu Ala Arg
            1230                1235                1240

GGG GCT GAG ACC CGT GGT TCC TCC AGG ATG AAG ACA TTT GAG GAA TTC   3795
Gly Ala Glu Thr Arg Gly Ser Ser Arg Met Lys Thr Phe Glu Glu Phe
        1245                1250                1255

CCC ATG ACC CCA ACG ACC TAC AAA GGC TCT GTG GAC AAC CAG ACA GAC   3843
Phe Met Thr Pro Thr Thr Tyr Lys Gly Ser Val Asp Asn Gln Thr Asp
    1260                1265                1270

AGT GGG ATG GTG CTG GCC TCG GAG GAG TTT GAG CAG ATA GAG AGC AGG   3891
Ser Gly Met Val Leu Ala Ser Glu Glu Phe Glu Gln Ile Glu Ser Arg
1275                1280                1285                1290

CAT AGA CAA GAA AGC GGC TTC AGG TAGCTGAAGC AGAGAGAGAG AAGGCAGCAT   3945
His Arg Gln Glu Ser Gly Phe Arg
                1295

ACGTCAGCAT TTTCTTCTCT GCACTTATAA GAAAGATCAA AGACTTTAAG ACTTTCGCTA 4005
TTTCTTCTAC TGCTATCTAC TACAAACTTC AAAGAGGAAC CAGGAGGACA AGAGGAGCAT 4065
GAAAGTGGAC AAGGAGTGTG ACCACTGAAG CACCACAGGG AGGGGTTAGG CCTCCGGATG 4125
ACTGCGGGCA GGCCTGGATA ATATCCAGCC TCCCACAAGA AGCTGGTGGA GCAGAGTGTT 4185
CCCTGACTCC TCCAAGGAAA GGGAGACGCC CTTTCATGGT CTGCTGAGTA ACAGGTGCCT 4245
TCCCAGACAC TGGCGTTACT GCTTGACCAA AGAGCCCTCA AGCGGCCCTT ATGCCAGCGT 4305
GACAGAGGGC TCACCTCTTG CCTTCTAGGT CACTTCTCAC AATGTCCCTT CAGCACCTGA 4365
CCCTGTGCCC GCCGATTATT CCTTGGTAAT ATGAGTAATA CATCAAAGAG TAGTATTAAA 4425
AGCTAATTAA TCATGTTTAT AAAAA                                       4450
```

FIG. 1F

Benign Node stained with anti-FLT-4 antibody:

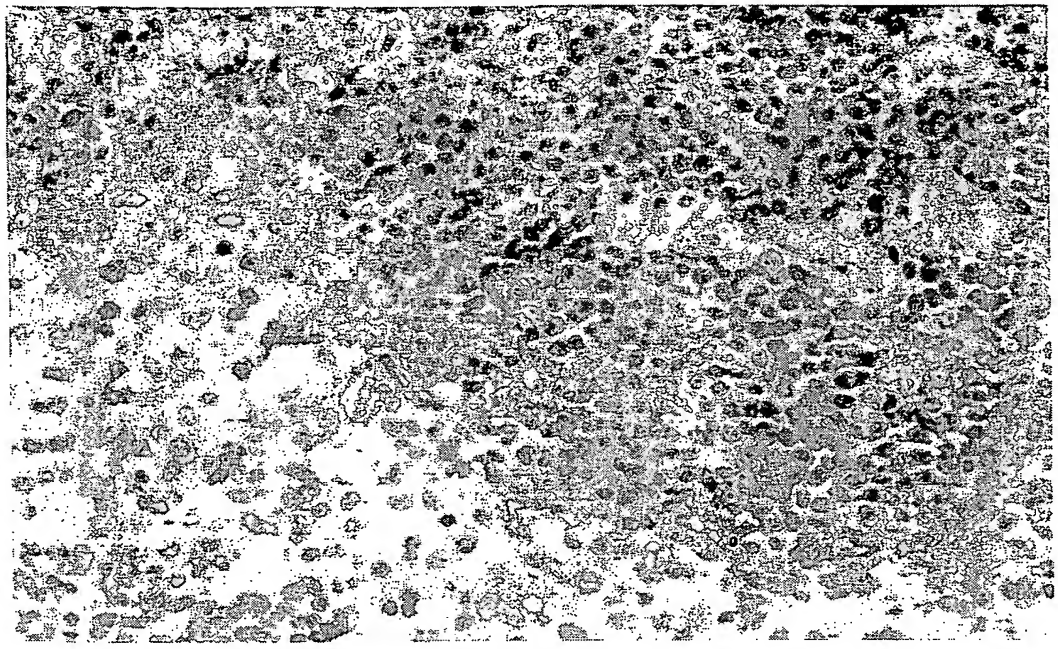

FIG.2A

BPH stained with anti-FLT-4:

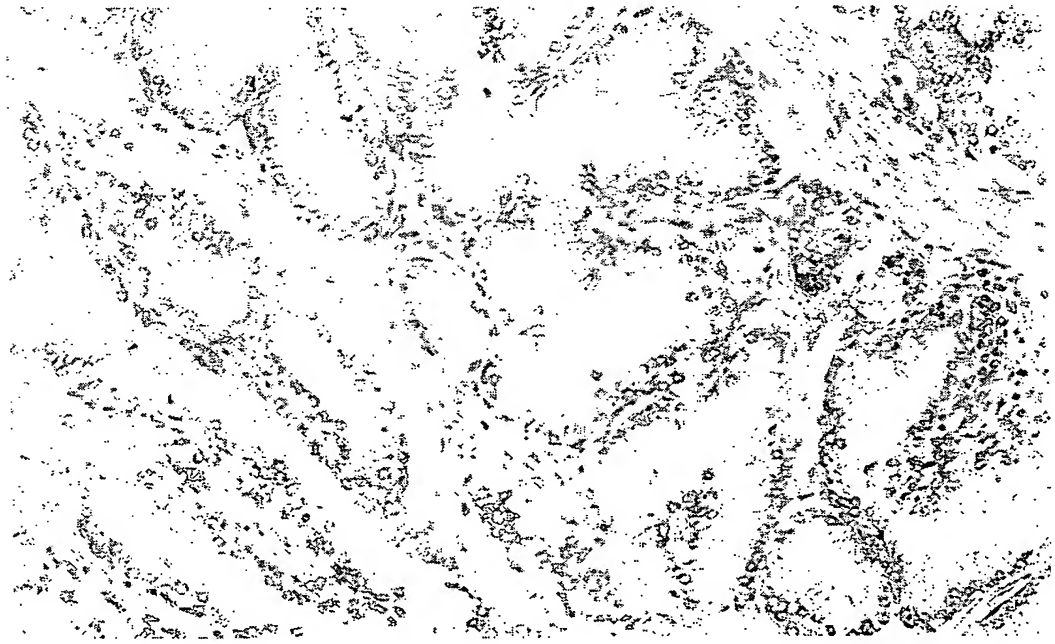

FIG.2B

Node with prostatic metastases stained with anti-FLT-4 antibody:

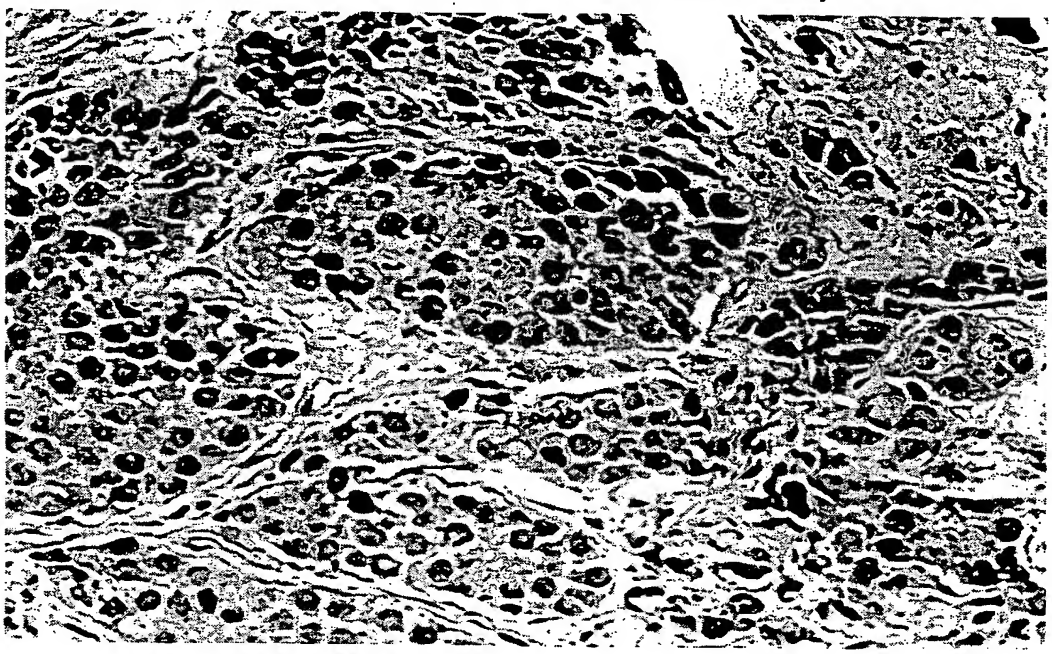

FIG.2C

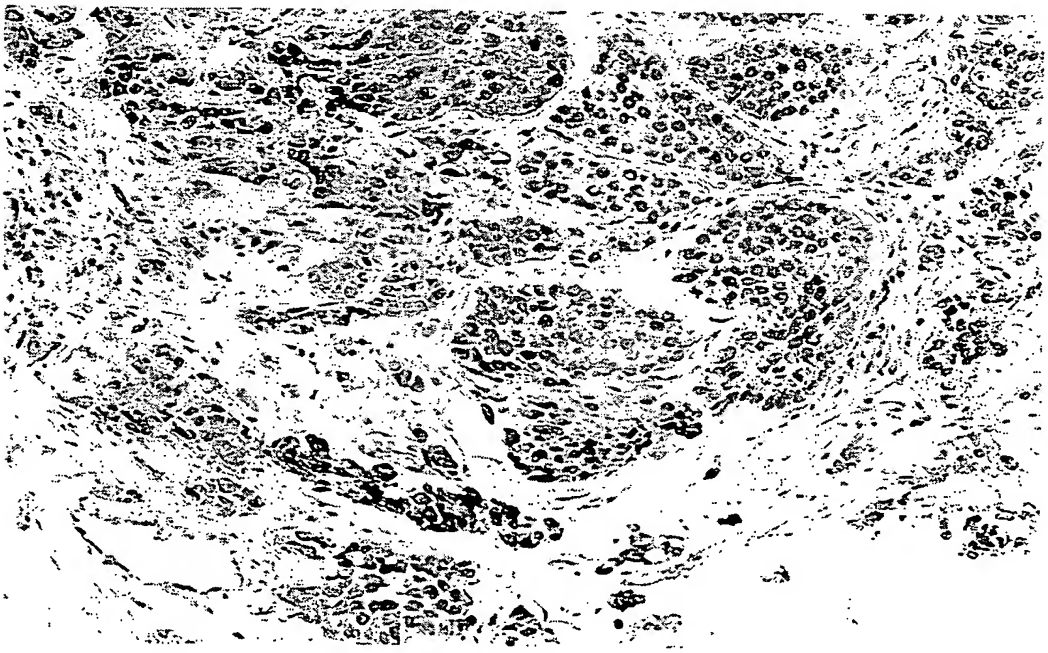

FIG.2D

BPH and extensive CaP stained with anti-FLT-4 showing positive reactivity in CaP and mostly negative reactivity in BPH:

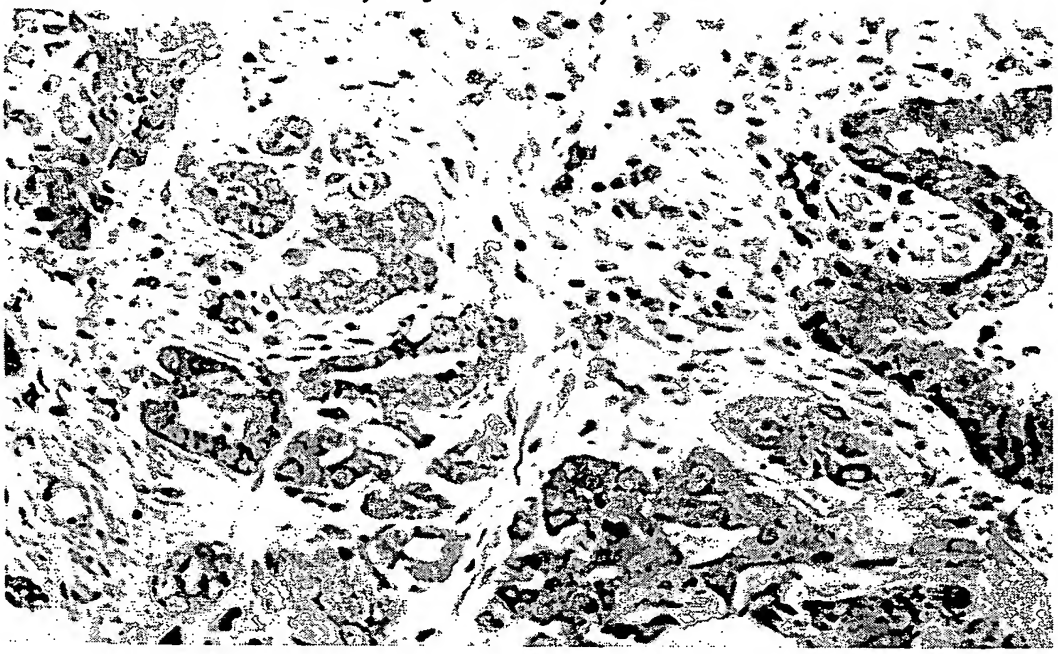

FIG.2E

Extensive CaP stained with anti-FLT-4:

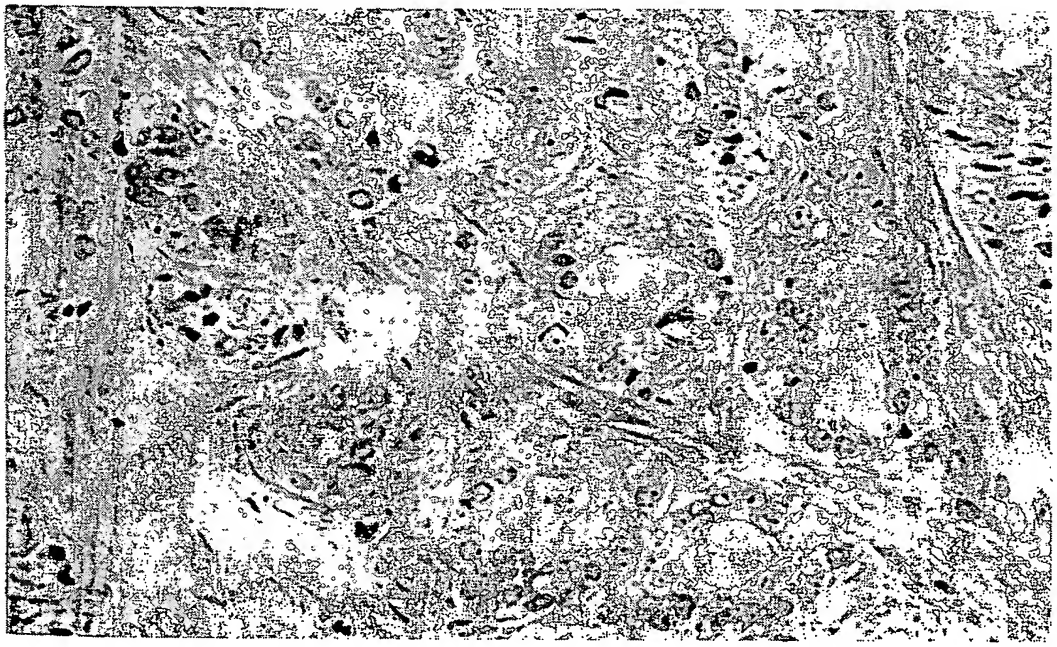

FIG.2F

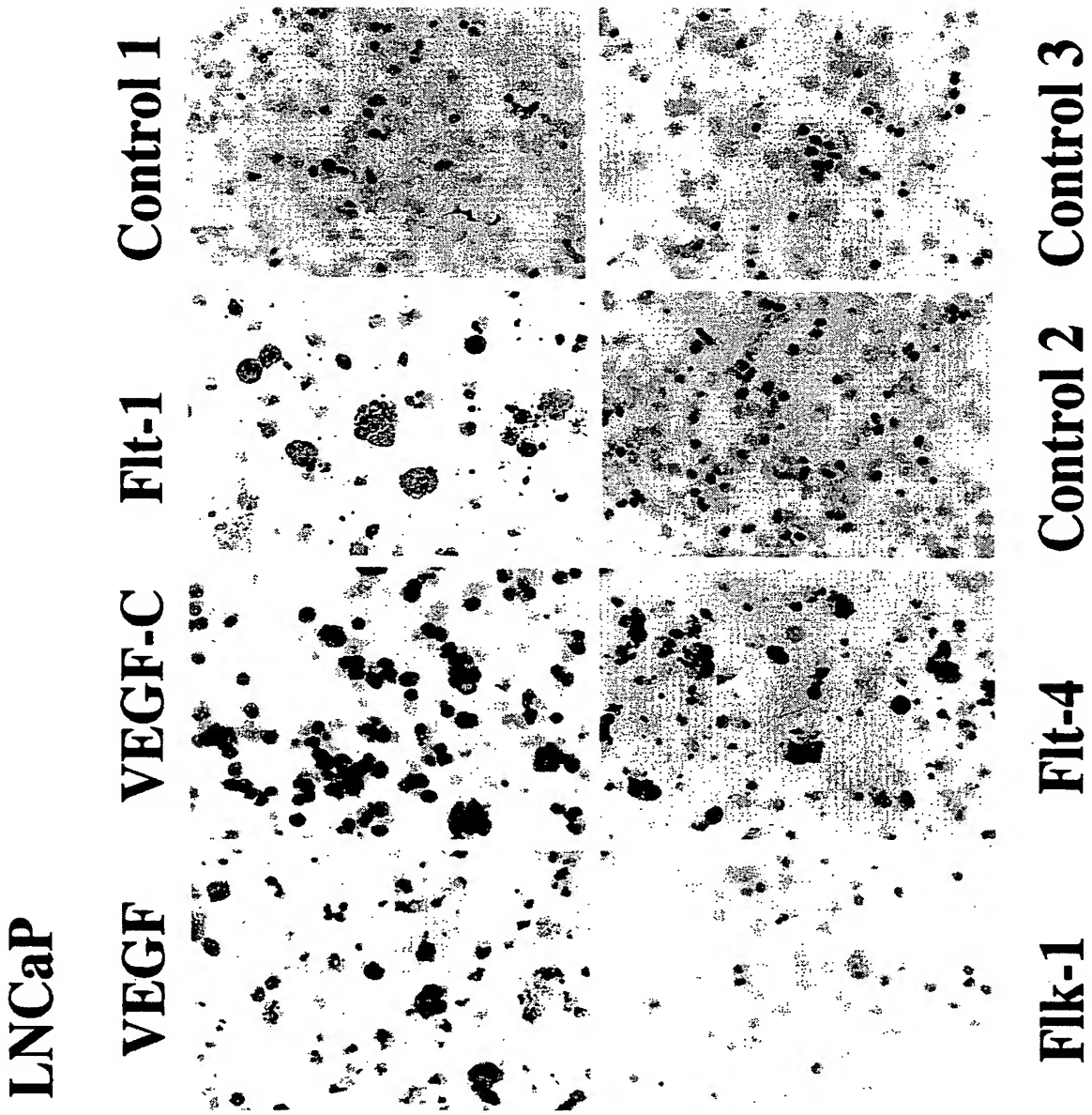
LNCaP
VEGF
VEGF-C
Flt-1
Control 1
Flk-1
Flt-4
Control 2
Control 3

FIG.3A

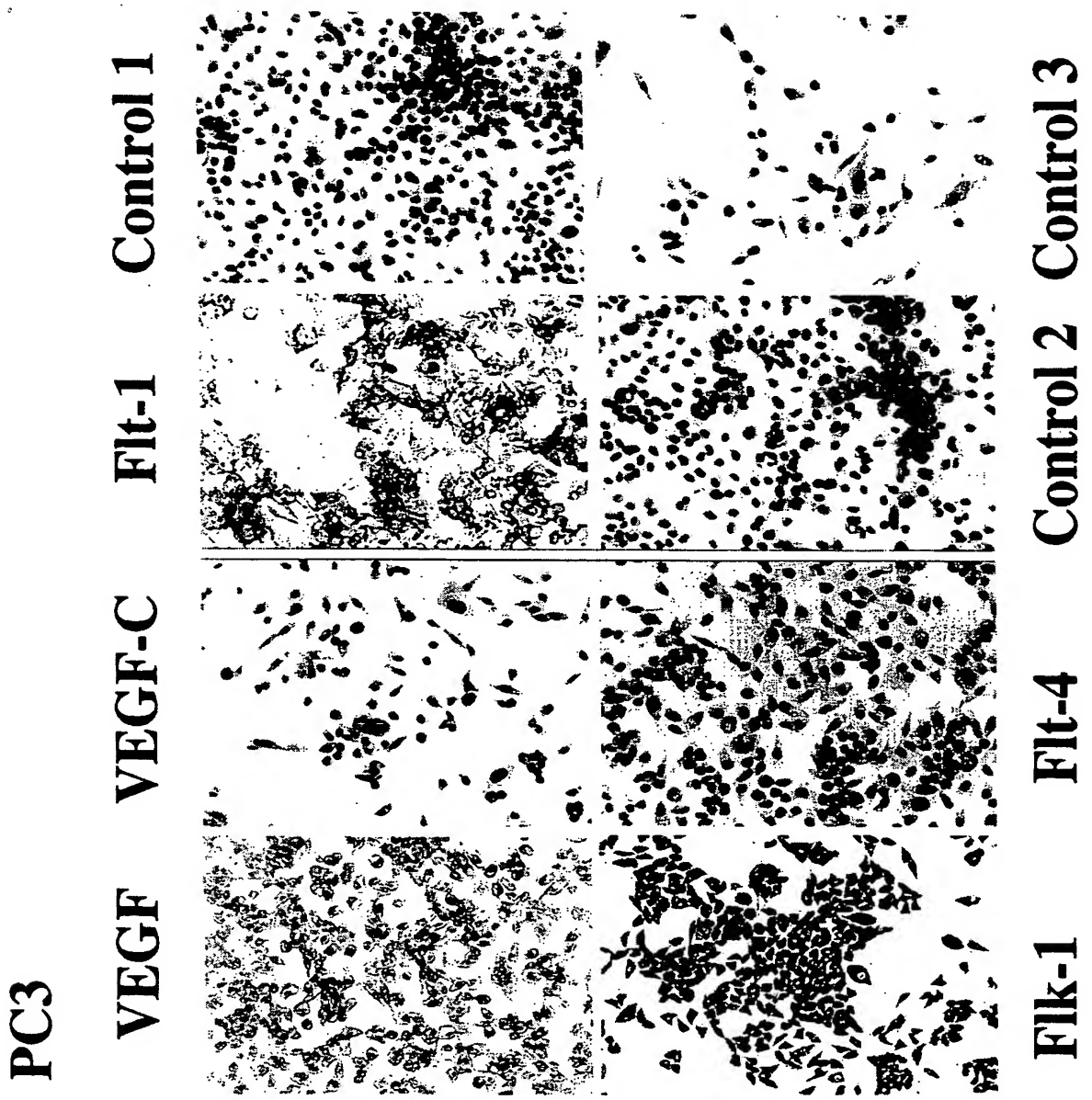

FIG.3B

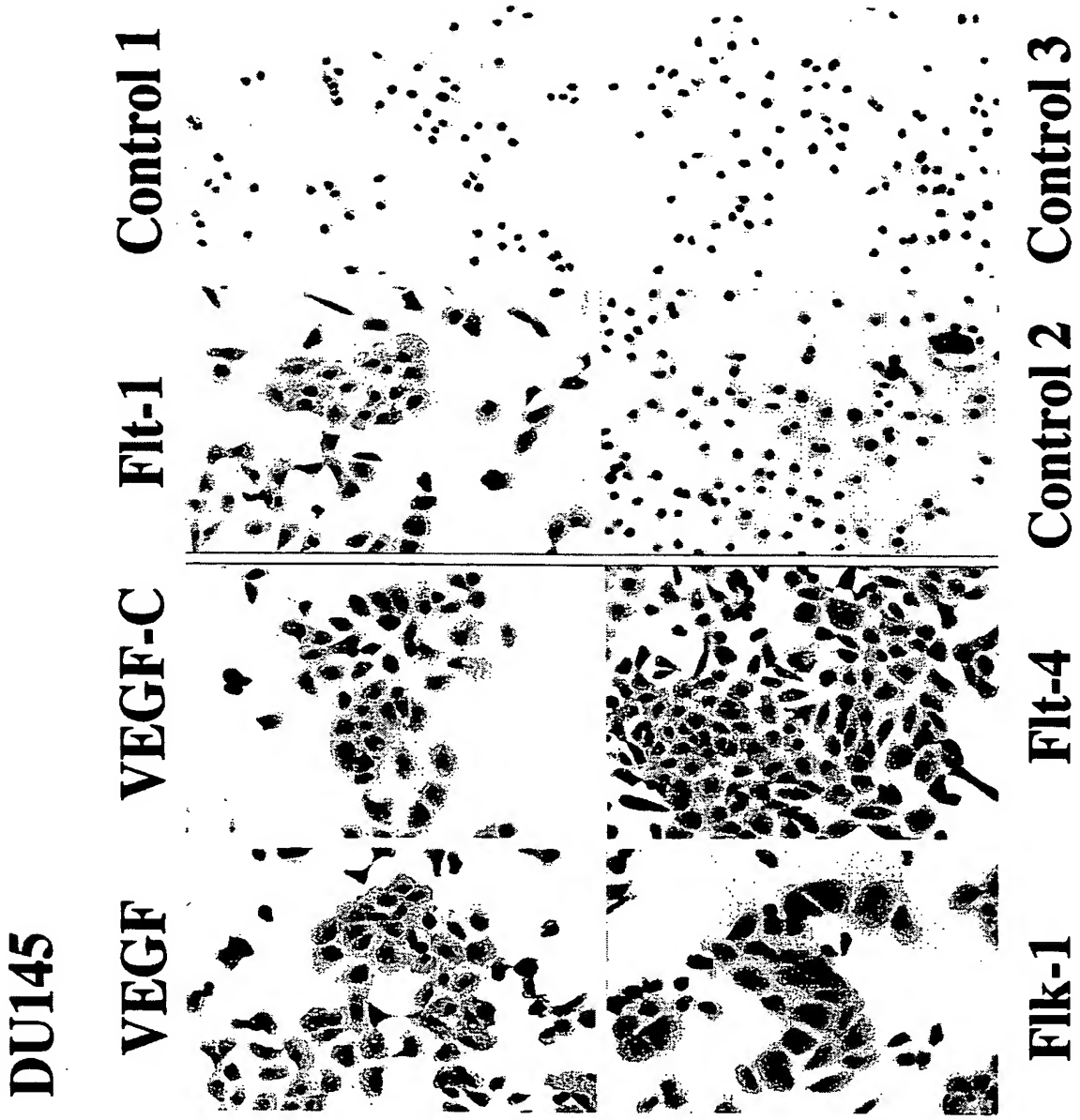
DU145
VEGF
VEGF-C
Flt-1
Control 1
Flk-1
Flt-4
Control 2
Control 3

FIG.3C

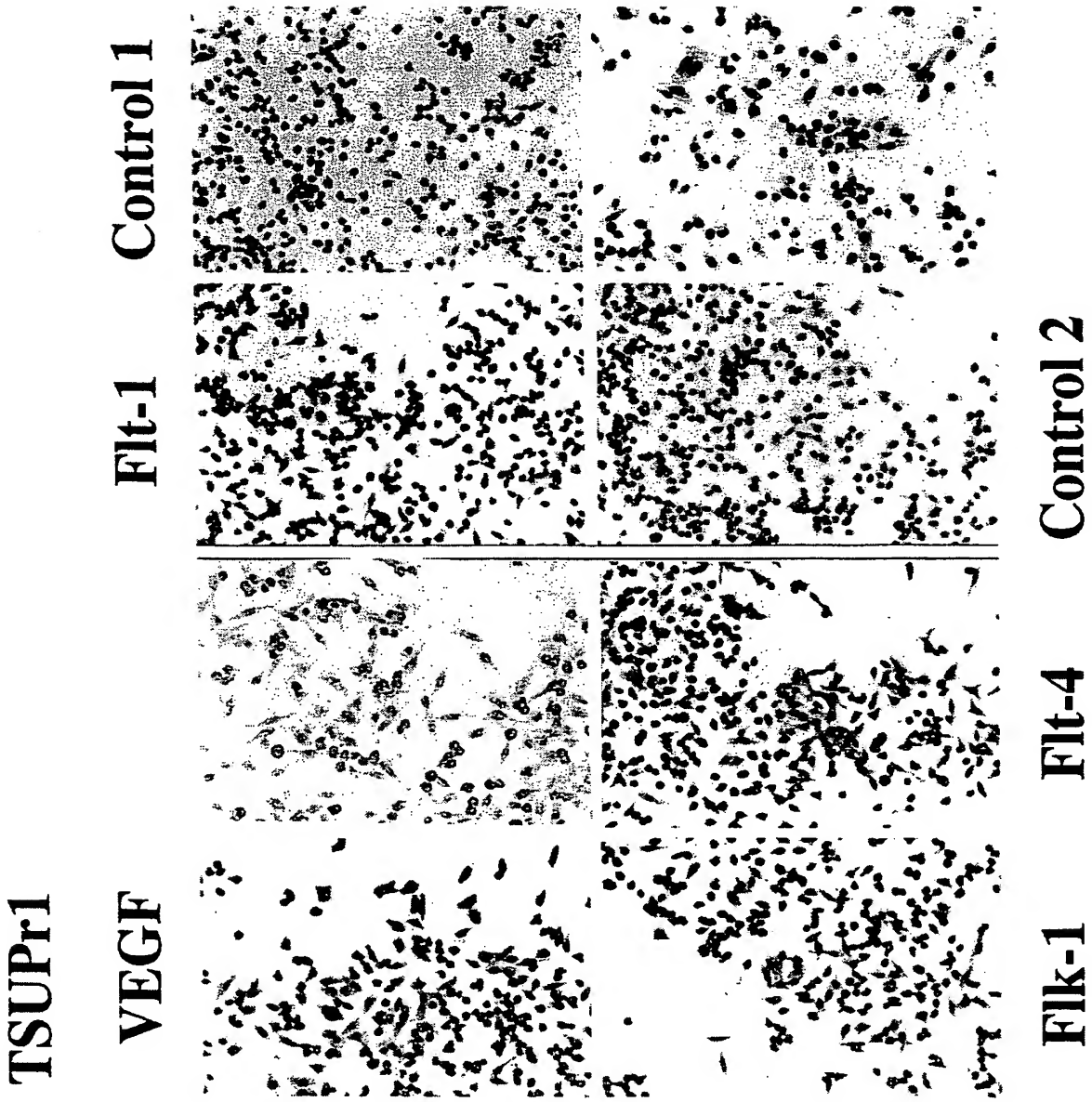

FIG.3D

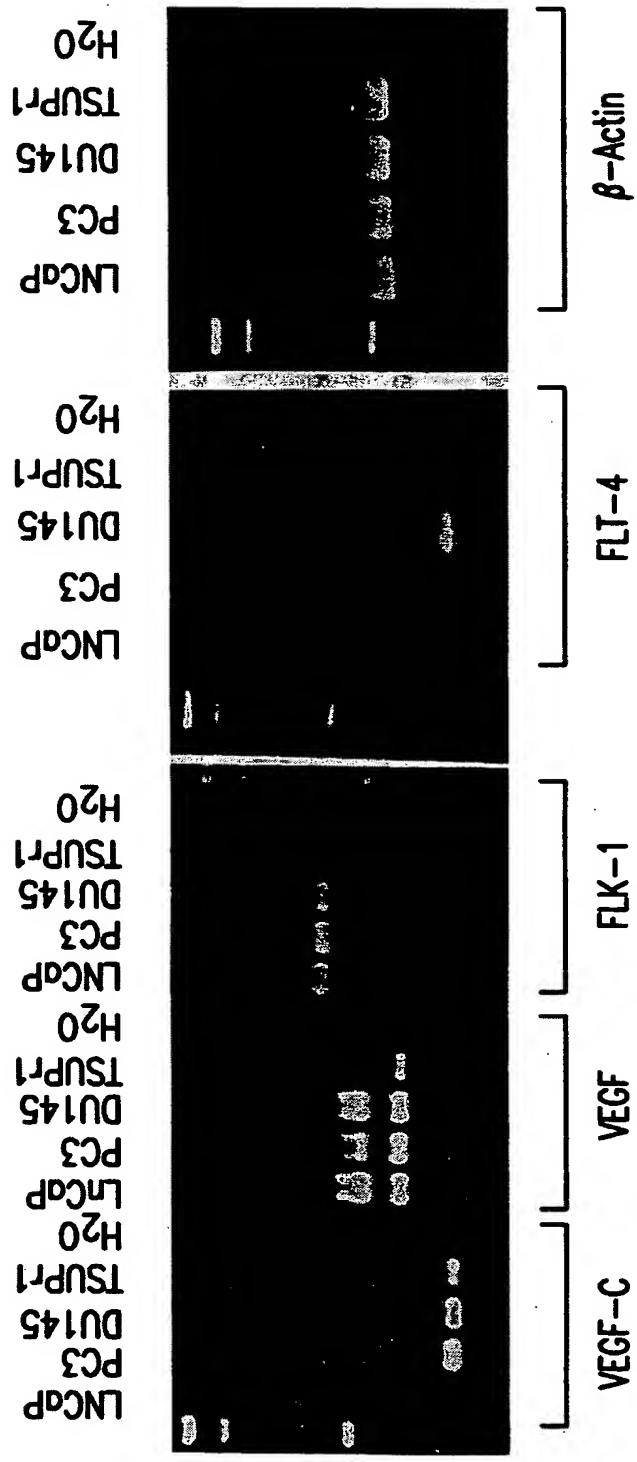

FIG.4

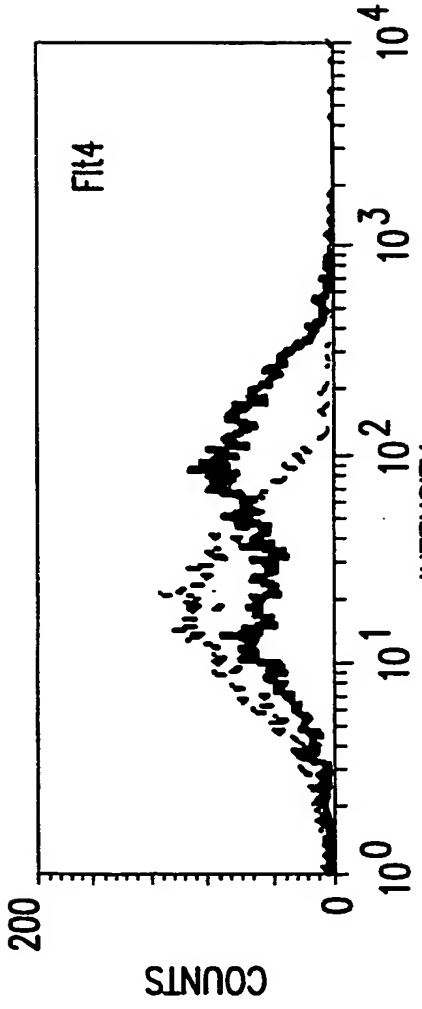

FIG.5

The dotted line shows the isotype control while the solid line shows binding with specific antibodies.

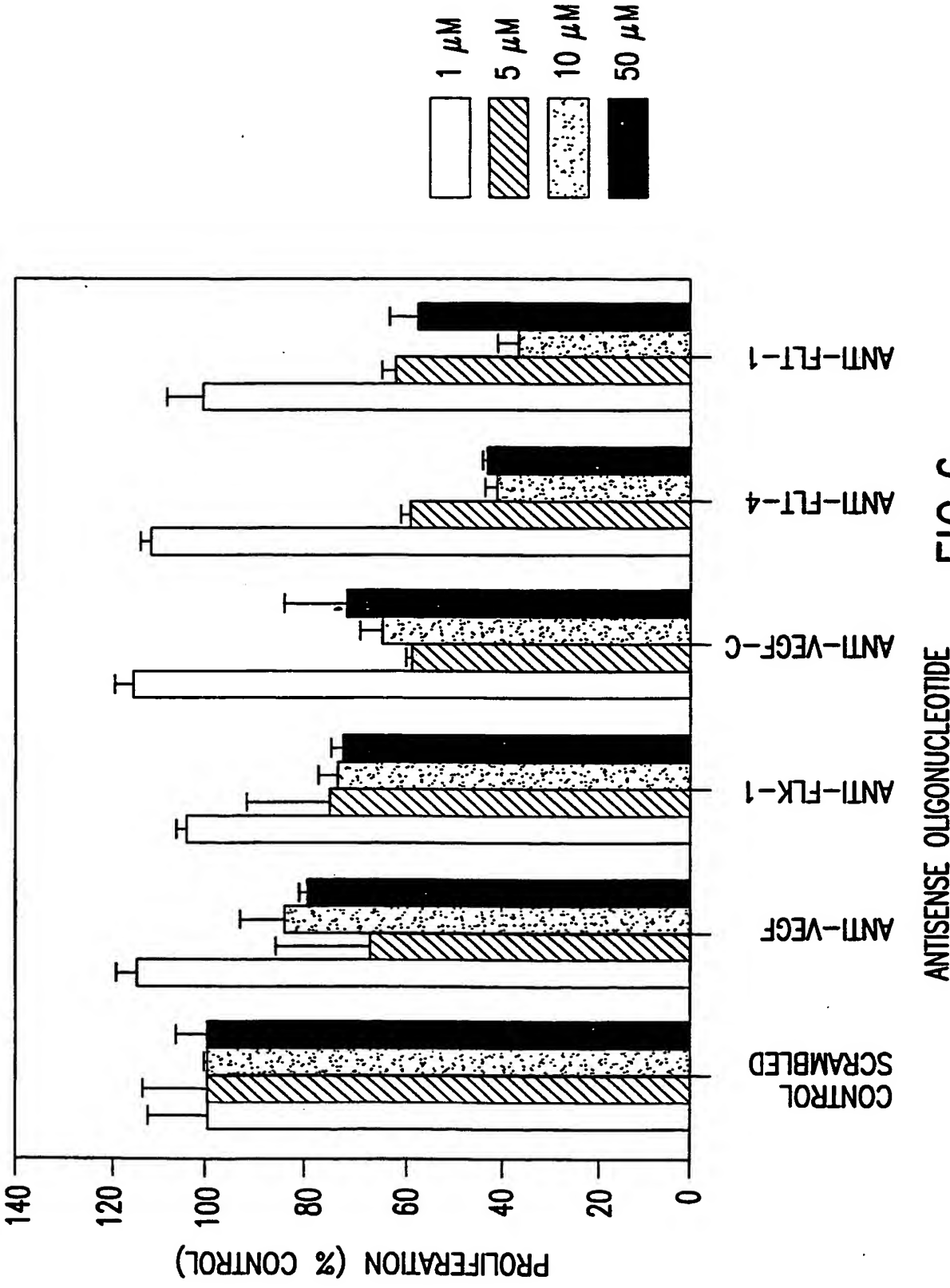
1 μM
5 μM
10 μM
50 μM
PROLIFERATION (% CONTROL)
0
20
40
60
80
100
120
140
CONTROL SCRAMBLED
ANTI-VEGF
ANTI-FLK-1
ANTI-VEGF-C
ANTI-FLT-4
ANTI-FLT-1
ANTISENSE OLIGONUCLEOTIDE

FIG.6